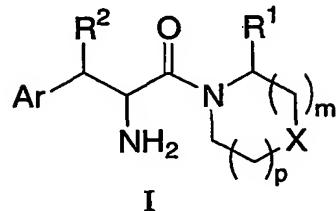


## WHAT IS CLAIMED IS:

## 1. A compound of structural formula I:



5 or a pharmaceutically acceptable salt thereof; wherein  
 each n is independently 0, 1, or 2;  
 m and p are independently 0 or 1;  
 q is 1 or 2;

10 X is  $\text{CH}_2$ , S,  $\text{CHF}$ , or  $\text{CF}_2$ ;

Ar is phenyl, unsubstituted or substituted with one to five  $\text{R}^3$  substituents;

15  $\text{R}^1$  is hydrogen or cyano;

20  $\text{R}^2$  is selected from the group consisting of

$\text{C}_{1-10}$  alkyl, wherein alkyl is unsubstituted or substituted with one to five substituents

independently selected from halogen or hydroxy,

$\text{C}_{2-10}$  alkenyl, wherein alkenyl is unsubstituted or substituted with one to five

25 substituents independently selected from halogen or hydroxy,

$(\text{CH}_2)_n$ -aryl, wherein aryl is unsubstituted or substituted with one to five substituents

independently selected hydroxy, halogen,  $\text{CO}_2\text{H}$ ,  $\text{C}_{1-6}$  alkyloxycarbonyl,  $\text{C}_{1-6}$  alkyl, and  $\text{C}_{1-6}$  alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens,

25  $(\text{CH}_2)_n$ -heteroaryl, wherein heteroaryl is unsubstituted or substituted with one to three substituents independently selected from hydroxy, halogen,  $\text{CO}_2\text{H}$ ,  $\text{C}_{1-6}$  alkyloxycarbonyl,  $\text{C}_{1-6}$  alkyl, and  $\text{C}_{1-6}$  alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens,

(CH<sub>2</sub>)<sub>n</sub>-heterocyclyl, wherein heterocyclyl is unsubstituted or substituted with one to three substituents independently selected from oxo, hydroxy, halogen, CO<sub>2</sub>H, C<sub>1-6</sub> alkyloxycarbonyl, C<sub>1-6</sub> alkyl, and C<sub>1-6</sub> alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens,

5 (CH<sub>2</sub>)<sub>n</sub>-C<sub>3-6</sub> cycloalkyl, wherein cycloalkyl is unsubstituted or substituted with one to three substituents independently selected from halogen, hydroxy, CO<sub>2</sub>H, C<sub>1-6</sub> alkyloxycarbonyl, C<sub>1-6</sub> alkyl, and C<sub>1-6</sub> alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens,

10 (CH<sub>2</sub>)<sub>n</sub>COOH,

(CH<sub>2</sub>)<sub>n</sub>COOC<sub>1-6</sub> alkyl,

(CH<sub>2</sub>)<sub>n</sub>CONR<sup>4</sup>R<sup>5</sup>, wherein R<sup>4</sup> and R<sup>5</sup> are independently selected from the group consisting of hydrogen, tetrazolyl, thiazolyl, (CH<sub>2</sub>)<sub>n</sub>-phenyl, (CH<sub>2</sub>)<sub>n</sub>-C<sub>3-6</sub> cycloalkyl, and C<sub>1-6</sub> alkyl, wherein alkyl is unsubstituted or substituted with one to five halogens and wherein phenyl and cycloalkyl are unsubstituted or substituted with one to five substituents independently selected from halogen, hydroxy, C<sub>1-6</sub> alkyl, and C<sub>1-6</sub> alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens;

15 or R<sup>4</sup> and R<sup>5</sup> together with the nitrogen atom to which they are attached form a heterocyclic ring selected from azetidine, pyrrolidine, piperidine, piperazine, and morpholine wherein said heterocyclic ring is unsubstituted or substituted with one to five substituents independently selected from halogen, hydroxy, C<sub>1-6</sub> alkyl, and C<sub>1-6</sub> alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens; and

20 wherein any methylene (CH<sub>2</sub>) carbon atom in R<sup>2</sup> is unsubstituted or substituted with one to two groups independently selected from halogen, hydroxy, C<sub>1-4</sub> alkyl, and C<sub>1-4</sub> alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens;

25 each R<sup>3</sup> is independently selected from the group consisting of

30 halogen,

cyano,

hydroxy,

C<sub>1-6</sub> alkyl, wherein alkyl is unsubstituted or substituted with one to five halogens,

C<sub>1-6</sub> alkoxy, wherein alkoxy is unsubstituted or substituted with one to five halogens,

phenyloxy, unsubstituted or substituted with one to five substituents independently selected from halogen, hydroxy, CO<sub>2</sub>H, cyano, C<sub>1</sub>-6 alkyloxycarbonyl, C<sub>1</sub>-6 alkyl, and C<sub>1</sub>-6 alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens;

5 (CH<sub>2</sub>)<sub>n</sub>-NR<sup>4</sup>R<sup>5</sup>,  
(CH<sub>2</sub>)<sub>n</sub>-CONR<sup>4</sup>R<sup>5</sup>,  
(CH<sub>2</sub>)<sub>n</sub>-OCONR<sup>4</sup>R<sup>5</sup>,  
(CH<sub>2</sub>)<sub>n</sub>-SO<sub>2</sub>NR<sup>4</sup>R<sup>5</sup>,  
(CH<sub>2</sub>)<sub>n</sub>-SO<sub>2</sub>R<sup>6</sup>,

10 (CH<sub>2</sub>)<sub>n</sub>-NR<sup>7</sup>SO<sub>2</sub>R<sup>6</sup>,  
(CH<sub>2</sub>)<sub>n</sub>-NR<sup>7</sup>CONR<sup>4</sup>R<sup>5</sup>,  
(CH<sub>2</sub>)<sub>n</sub>-NR<sup>7</sup>COR<sup>7</sup>,  
(CH<sub>2</sub>)<sub>n</sub>-NR<sup>7</sup>CO<sub>2</sub>R<sup>6</sup>,  
(CH<sub>2</sub>)<sub>n</sub>-COOH,

15 (CH<sub>2</sub>)<sub>n</sub>-COOC<sub>1</sub>-<sub>6</sub> alkyl,  
(CH<sub>2</sub>)<sub>q</sub>-aryl, wherein aryl is unsubstituted or substituted with one to five substituents independently selected from halogen, hydroxy, CO<sub>2</sub>H, C<sub>1</sub>-6 alkyloxycarbonyl, C<sub>1</sub>-6 alkyl, C<sub>3</sub>-6 cycloalkyl, and C<sub>1</sub>-6 alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens,

20 (CH<sub>2</sub>)<sub>q</sub>-heteroaryl, wherein heteroaryl is unsubstituted or substituted with one to three substituents independently selected from hydroxy, halogen, CO<sub>2</sub>H, C<sub>1</sub>-6 alkyloxycarbonyl, C<sub>1</sub>-6 alkyl, C<sub>3</sub>-6 cycloalkyl, and C<sub>1</sub>-6 alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens,

25 (CH<sub>2</sub>)<sub>q</sub>-heterocyclyl, wherein heterocyclyl is unsubstituted or substituted with one to three substituents independently selected from oxo, hydroxy, halogen, CO<sub>2</sub>H, C<sub>1</sub>-6 alkyloxycarbonyl, C<sub>1</sub>-6 alkyl, C<sub>3</sub>-6 cycloalkyl, and C<sub>1</sub>-6 alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens,

(CH<sub>2</sub>)<sub>n</sub>-C<sub>3</sub>-<sub>6</sub> cycloalkyl, wherein cycloalkyl is unsubstituted or substituted with one to three substituents independently selected from halogen, hydroxy, C<sub>1</sub>-6 alkyl, and C<sub>1</sub>-6 alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens,

30 wherein any methylene (CH<sub>2</sub>) carbon atom in R<sup>3</sup> is unsubstituted or substituted with one to two groups independently selected from halogen, hydroxy, C<sub>1</sub>-4 alkyl, and C<sub>1</sub>-4

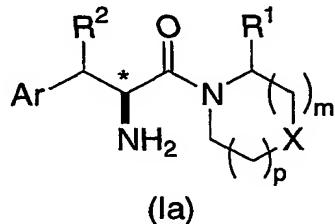
alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens;

5      R<sup>6</sup> is independently selected from the group consisting of tetrazolyl, thiazolyl, (CH<sub>2</sub>)<sub>n</sub>-phenyl, (CH<sub>2</sub>)<sub>n</sub>-C<sub>3</sub>-6 cycloalkyl, and C<sub>1</sub>-6 alkyl, wherein alkyl is unsubstituted or substituted with one to five halogens and wherein phenyl and cycloalkyl are unsubstituted or substituted with one to five substituents independently selected from halogen, hydroxy, C<sub>1</sub>-6 alkyl, and C<sub>1</sub>-6 alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens, and wherein any methylene (CH<sub>2</sub>) carbon atom in R<sup>6</sup> is unsubstituted or substituted with one to two groups

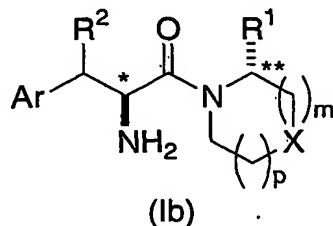
10     independently selected from halogen, hydroxy, and C<sub>1</sub>-4 alkyl unsubstituted or substituted with one to five halogens; and

each R<sup>7</sup> is hydrogen or R<sup>6</sup>.

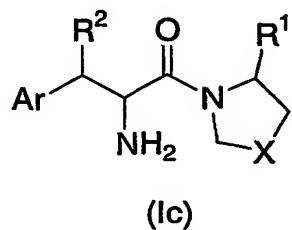
15     2.     The compound of Claim 1 wherein the carbon atom marked with an \* has the stereochemical configuration as depicted in formula Ia:



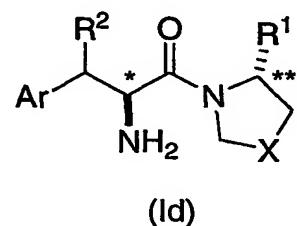
3.     The compound of Claim 2 wherein the carbon atom attached to R<sup>1</sup> marked with an \*\* has the stereochemical configuration as depicted in formula Ib:



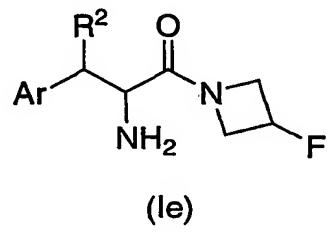
4. The compound of Claim 1 of the structural formula Ic:



5. The compound of Claim 4 wherein the carbon atom marked with an \* and  
5 the carbon atom marked with an \*\* have the stereochemical configurations as depicted in  
formula Id:

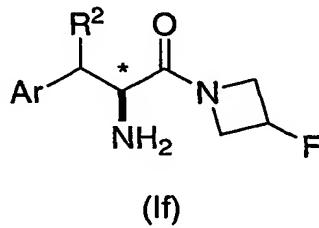


6. The compound of Claim 1 of the structural formula Ie

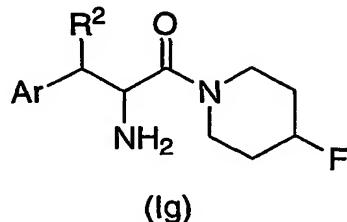


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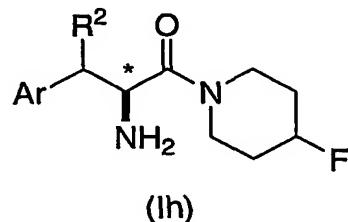
7. The compound of Claim 6 wherein the carbon atom marked with an \* has  
the stereochemical configuration as depicted in formula If:



8. The compound of Claim 1 of the structural formula Ig



9. The compound of Claim 8 wherein the carbon atom marked with an \* has the stereochemical configuration as depicted in formula Ih:



5

10. The compound of Claim 1 wherein R<sup>2</sup> is selected from the group consisting of

C<sub>1-6</sub> alkyl, wherein alkyl is unsubstituted or substituted with one to five substituents independently selected from halogen or hydroxy,

10 C<sub>2-6</sub> alkenyl, wherein alkenyl is unsubstituted or substituted with one to five substituents

independently selected from halogen or hydroxy,

(CH<sub>2</sub>)<sub>n</sub>-C<sub>3-6</sub> cycloalkyl, wherein cycloalkyl is unsubstituted or substituted with one to three substituents independently selected from halogen, hydroxy, CO<sub>2</sub>H, C<sub>1-6</sub> alkyloxycarbonyl, C<sub>1-6</sub> alkyl, and C<sub>1-6</sub> alkoxy, wherein alkyl and alkoxy are

15 unsubstituted or substituted with one to five halogens,

(CH<sub>2</sub>)<sub>n</sub>COOH,

(CH<sub>2</sub>)<sub>n</sub>COOC<sub>1-6</sub> alkyl, and

16 (CH<sub>2</sub>)<sub>n</sub>CONR<sup>4</sup>R<sup>5</sup>, wherein R<sup>4</sup> and R<sup>5</sup> are independently selected from the group consisting of hydrogen, tetrazolyl, thiazolyl, (CH<sub>2</sub>)<sub>n</sub>-phenyl, (CH<sub>2</sub>)<sub>n</sub>-C<sub>3-6</sub>

20 cycloalkyl, and C<sub>1-6</sub> alkyl, wherein alkyl is unsubstituted or substituted with one to five halogens and wherein phenyl and cycloalkyl are unsubstituted or substituted with one to five substituents independently selected from halogen, hydroxy, C<sub>1-6</sub> alkyl, and C<sub>1-6</sub> alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens;

5 or R<sup>4</sup> and R<sup>5</sup> together with the nitrogen atom to which they are attached form a heterocyclic ring selected from pyrrolidine, piperidine, piperazine, and morpholine wherein said heterocyclic ring is unsubstituted or substituted with one to five substituents independently selected from halogen, hydroxy, C<sub>1-6</sub> alkyl, and C<sub>1-6</sub> alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens; and

10 wherein any methylene (CH<sub>2</sub>) carbon atom in R<sup>2</sup> is unsubstituted or substituted with one to two groups independently selected from halogen, hydroxy, C<sub>1-4</sub> alkyl, and C<sub>1-4</sub> alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens.

15 11. The compound of Claim 10 wherein R<sup>2</sup> is selected from the group consisting of

16 C<sub>1-3</sub> alkyl, wherein alkyl is unsubstituted or substituted with one to five substituents independently selected from halogen or hydroxy,

20 CH<sub>2</sub>-C<sub>3-6</sub> cycloalkyl,

COOH,

COOC<sub>1-6</sub> alkyl, and

25 CONR<sup>4</sup>R<sup>5</sup>, wherein R<sup>4</sup> and R<sup>5</sup> are independently selected from the group consisting of hydrogen, tetrazolyl, thiazolyl, (CH<sub>2</sub>)<sub>n</sub>-phenyl, (CH<sub>2</sub>)<sub>n</sub>-C<sub>3-6</sub> cycloalkyl, and C<sub>1-6</sub> alkyl, wherein alkyl is unsubstituted or substituted with one to five halogens and wherein phenyl and cycloalkyl are unsubstituted or substituted with one to five substituents independently selected from halogen, hydroxy, C<sub>1-6</sub> alkyl, and C<sub>1-6</sub> alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens;

30 or R<sup>4</sup> and R<sup>5</sup> together with the nitrogen atom to which they are attached form a heterocyclic ring selected from pyrrolidine, piperidine, piperazine, and morpholine wherein said heterocyclic ring is unsubstituted or substituted with one to five substituents independently selected from halogen, hydroxy, C<sub>1-6</sub> alkyl, and C<sub>1-6</sub> alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens.

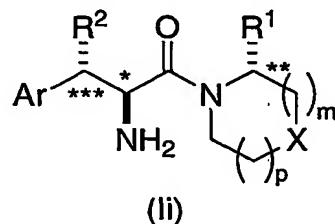
35 12. The compound of Claim 11 wherein R<sup>2</sup> is selected from the group consisting of

methyl,

ethyl,

5                   CH<sub>2</sub>-cyclopropyl,  
                   COOH,  
                   COOMe,  
                   COOEt,  
                   CONMe<sub>2</sub>,  
                   CONH<sub>2</sub>,  
                   CONHMe,  
                   CONHEt,  
                   pyrrolidin-1-ylcarbonyl,  
 10                azetidin-1-ylcarbonyl, and  
                   [(tetrazol-5-yl)amino]carbonyl.

13.       The compound of Claim 1 wherein the carbon atom marked with an \*, the carbon atom attached to R<sup>1</sup> marked with an \*\*, and the carbon atom attached to R<sup>2</sup> marked with 15       an \*\*\* have the stereochemical configurations as depicted in formula II:



R<sup>2</sup> is selected from the group consisting of

C<sub>1-6</sub> alkyl, wherein alkyl is unsubstituted or substituted with one to five substituents

independently selected from halogen or hydroxy,

20               (CH<sub>2</sub>)<sub>n</sub>-C<sub>3-6</sub> cycloalkyl,

COOH,

COOC<sub>1-6</sub>alkyl, and

CONR<sup>4</sup>R<sup>5</sup>, wherein R<sup>4</sup> and R<sup>5</sup> are independently selected from the group consisting of hydrogen, tetrazolyl, thiazolyl, (CH<sub>2</sub>)<sub>n</sub>-phenyl, (CH<sub>2</sub>)<sub>n</sub>-C<sub>3-6</sub> cycloalkyl, and C<sub>1-6</sub>

25               alkyl, wherein alkyl is unsubstituted or substituted with one to five halogens and wherein phenyl and cycloalkyl are unsubstituted or substituted with one to five substituents independently selected from halogen, hydroxy, C<sub>1-6</sub> alkyl, and C<sub>1-6</sub> alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens;

5 or wherein R<sup>4</sup> and R<sup>5</sup> together with the nitrogen atom to which they are attached form a heterocyclic ring selected from pyrrolidine, piperidine, piperazine, and morpholine wherein said heterocyclic ring is unsubstituted or substituted with one to five substituents independently selected from halogen, hydroxy, C<sub>1</sub>-6 alkyl, and C<sub>1</sub>-6 alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens; and

each R<sup>3</sup> is independently selected from the group consisting of:

10 halogen,

hydroxy,

C<sub>1</sub>-6 alkyl, wherein alkyl is unsubstituted or substituted with one to five halogens, C<sub>1</sub>-6 alkoxy, wherein alkoxy is unsubstituted or substituted with one to five halogens, phenoxy, unsubstituted or substituted with one to three substituents independently selected from halogen, hydroxy, cyano, C<sub>1</sub>-6 alkyl, and C<sub>1</sub>-6 alkoxy, wherein

15 alkyl and alkoxy are unsubstituted or substituted with one to five halogens; and (CH<sub>2</sub>)<sub>n</sub>-C<sub>3</sub>-6 cycloalkyl, wherein cycloalkyl is unsubstituted or substituted with one to three substituents independently selected from halogen, hydroxy, C<sub>1</sub>-6 alkyl, and C<sub>1</sub>-6 alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens.

20

14. The compound of Claim 13 wherein R<sup>2</sup> is selected from the group consisting of

methyl,

ethyl,

25 CH<sub>2</sub>-cyclopropyl,

COOH,

COOMe,

COOEt,

CONMe<sub>2</sub>,

30 CONH<sub>2</sub>,

CONHMe,

CONH<sub>2</sub>Et,

pyrrolidin-1-ylcarbonyl,

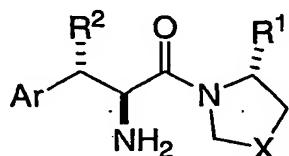
azetidin-1-ylcarbonyl, and

[(tetrazol-5-yl)amino]carbonyl.

15. The compound of Claim 14 wherein R<sup>3</sup> is selected from the group consisting of:

- 5       fluoro,
- chloro,
- bromo,
- trifluoromethyl,
- trifluoromethoxy, and
- 10      methoxy.

16. The compound of Claim 1 of the structural formula Ij



(Ij)

wherein X is CH<sub>2</sub>, S, CHF, or CF<sub>2</sub>;

- 15      Ar is phenyl, unsubstituted or substituted with one to five R<sup>3</sup> substituents;
- R<sup>1</sup> is hydrogen or cyano;

R<sup>2</sup> is selected from the group consisting of

C<sub>1-6</sub> alkyl, wherein alkyl is unsubstituted or substituted with one to five substituents

- 20      independently selected from halogen or hydroxy,
- (CH<sub>2</sub>)<sub>n</sub>-C<sub>3-6</sub> cycloalkyl,
- COOH,
- COOC<sub>1-6</sub> alkyl, and

- 25      CONR<sup>4</sup>R<sup>5</sup>, wherein R<sup>4</sup> and R<sup>5</sup> are independently selected from the group consisting of hydrogen, tetrazolyl, thiazolyl, (CH<sub>2</sub>)<sub>n</sub>-phenyl, (CH<sub>2</sub>)<sub>n</sub>-C<sub>3-6</sub> cycloalkyl, and C<sub>1-6</sub> alkyl, wherein alkyl is unsubstituted or substituted with one to five halogens and wherein phenyl and cycloalkyl are unsubstituted or substituted with one to five substituents independently selected from halogen, hydroxy, C<sub>1-6</sub> alkyl, and C<sub>1-6</sub>

alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens;

5 or R<sup>4</sup> and R<sup>5</sup> together with the nitrogen atom to which they are attached form a heterocyclic ring selected from pyrrolidine, piperidine, piperazine, and morpholine wherein said heterocyclic ring is unsubstituted or substituted with one to five substituents independently selected from halogen, hydroxy, C<sub>1-6</sub> alkyl, and C<sub>1-6</sub> alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens; and

10 each R<sup>3</sup> is independently selected from the group consisting of:

halogen,

C<sub>1-6</sub> alkyl, wherein alkyl is unsubstituted or substituted with one to five halogens,

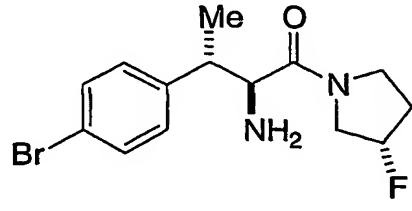
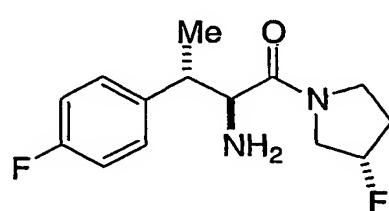
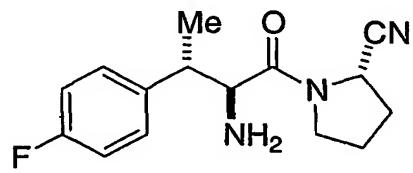
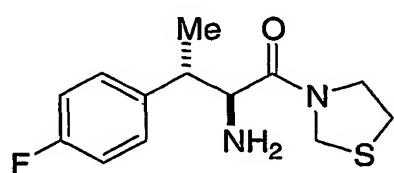
C<sub>1-6</sub> alkoxy, wherein alkoxy is unsubstituted or substituted with one to five halogens,

15 phenoxy, unsubstituted or substituted with one to three substituents

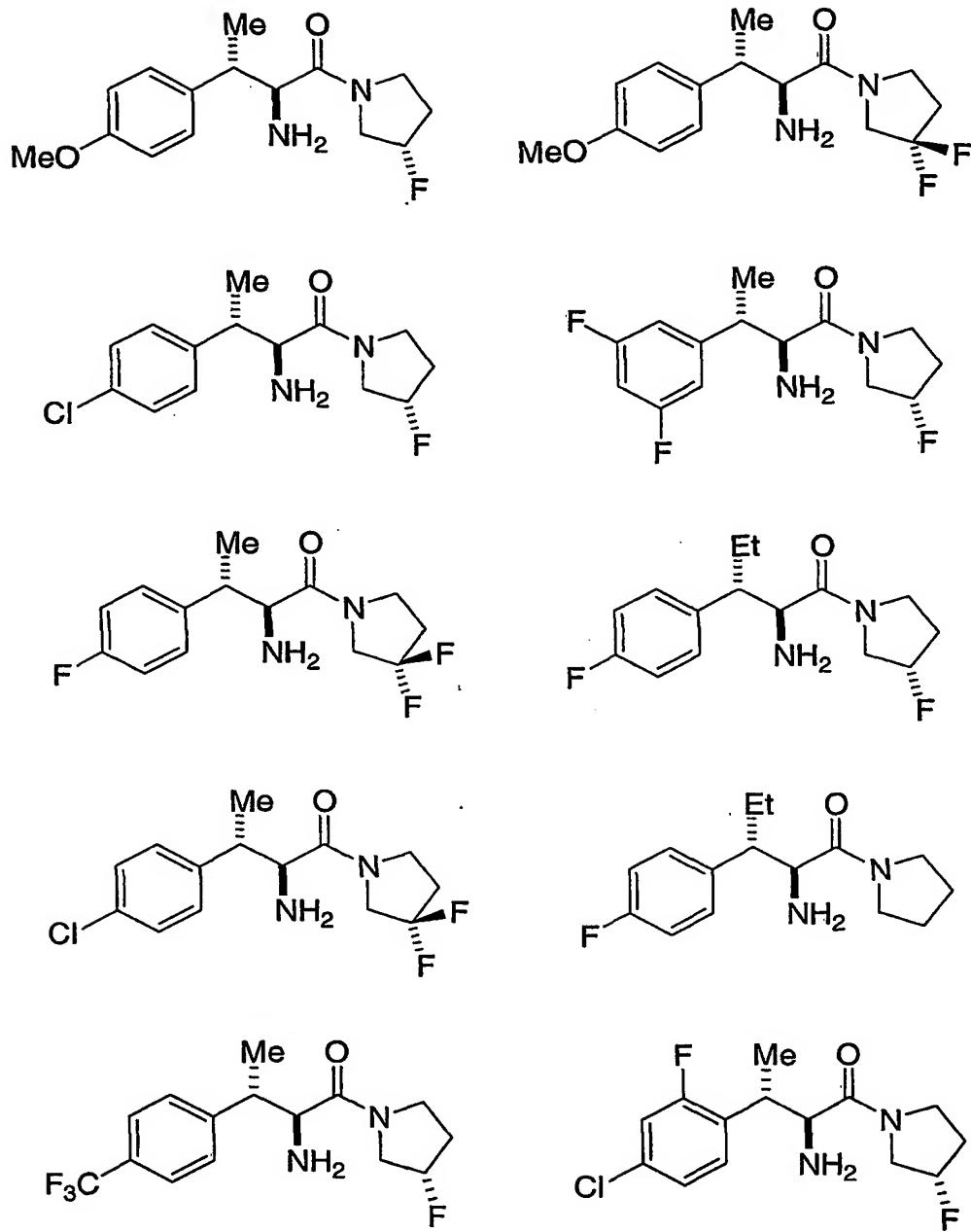
independently selected from halogen and cyano, and phenyl(CH<sub>2</sub>)<sub>n</sub>CON(Me)-, wherein phenyl is unsubstituted or substituted with one to three substituents independently selected from halogen, trifluoromethyl, and C<sub>1-4</sub> alkyl.

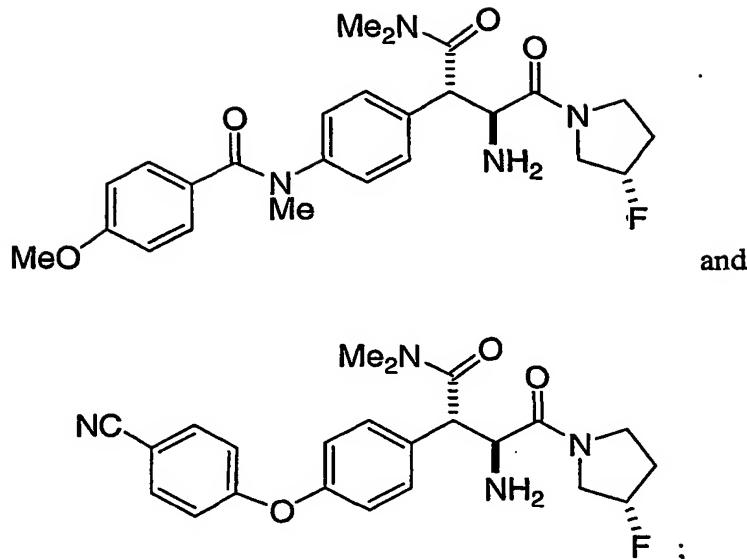
20

17. The compound of Claim 16 of the structural formula selected from the group consisting of



25





or a pharmaceutically acceptable salt thereof.

5 18. A pharmaceutical composition which comprises a compound of Claim 1 and a pharmaceutically acceptable carrier.

10 19. A method for inhibiting dipeptidyl peptidase-IV enzyme activity in a mammal in need thereof which comprises the administration to the mammal of an effective amount of a compound of Claim 1.

15 20. A method for treating diabetes in a mammal in need thereof which comprises the administration to the mammal of a therapeutically effective amount of a compound of Claim 1.

21. A method for treating non-insulin dependent (Type 2) diabetes in a mammal in need thereof which comprises the administration to the mammal of a therapeutically effective amount of a compound of Claim 1.

20 22. A method for treating hyperglycemia in a mammal in need thereof which comprises the administration to the mammal of a therapeutically effective amount of a compound of Claim 1.

23. A method for treating obesity in a mammal in need thereof which comprises the administration to the mammal of a therapeutically effective amount of a compound of Claim 1.

5 24. A method for treating one or more lipid disorders selected from the group of dyslipidemia, hyperlipidemia, hypertriglyceridemia, hypercholesterolemia, low HDL and high LDL in a mammal in need thereof which comprises the administration to the mammal of a therapeutically effective amount of a compound of Claim 1.

10 25. A method for treating in a mammal in need thereof one or more conditions selected from the group consisting of (1) hyperglycemia, (2) low glucose tolerance, (3) insulin resistance, (4) obesity, (5) lipid disorders, (6) dyslipidemia, (7) hyperlipidemia, (8) hypertriglyceridemia, (9) hypercholesterolemia, (10) low HDL levels, (11) high LDL levels, (12) atherosclerosis and its sequelae, (13) vascular restenosis, (14) irritable bowel syndrome, (15) inflammatory bowel disease, including Crohn's disease and ulcerative colitis, (16) other inflammatory conditions, (17) pancreatitis, (18) abdominal obesity, (19) neurodegenerative disease, (20) retinopathy, (21) nephropathy, (22) neuropathy, (23) Syndrome X, (24) ovarian hyperandrogenism (polycystic ovarian syndrome), and other disorders where insulin resistance is a component, wherein the method comprises the administration to the mammal a therapeutically effective amount of a compound of Claim 1.

26. The pharmaceutical composition of Claim 18 further comprising one or more additional active ingredients selected from the group consisting of:

(a) a second dipeptidyl peptidase IV inhibitor;

25 (b) an insulin sensitizer selected from the group consisting of a PPAR $\gamma$  agonist, a PPAR $\alpha/\gamma$  dual agonist, a PPAR $\alpha$  agonist, a biguanide, and a protein tyrosine phosphatase-1B inhibitor;

(c) an insulin or insulin mimetic;

30 (d) a sulfonylurea or other insulin secretagogue;

(e) an  $\alpha$ -glucosidase inhibitor;

(f) a glucagon receptor antagonist;

(g) GLP-1, a GLP-1 mimetic, or a GLP-1 receptor agonist;

(h) GIP, a GIP mimetic, or a GIP receptor agonist;

(i) PACAP, a PACAP mimetic, or a PACAP receptor agonist;

(j) a cholesterol lowering agent such as (i) HMG-CoA reductase inhibitor, (ii) sequestrant, (iii) nicotinyl alcohol, nicotinic acid or a salt thereof, (iv) PPAR $\alpha$  agonist, (v) PPAR $\alpha/\gamma$  dual agonist, (vi) inhibitor of cholesterol absorption, (vii) acyl CoA:cholesterol acyltransferase inhibitor, and (viii) anti-oxidant;

5 (k) a PPAR $\delta$  agonist;  
(l) an antiobesity compound;  
(m) an ileal bile acid transporter inhibitor;  
(n) an anti-inflammatory agent; and  
(o) an antihypertensive agent.

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27. The pharmaceutical composition of Claim 26 wherein the PPAR $\alpha/\gamma$  dual agonist is KRP-297.

15 28. A method of treating diabetes in a mammal in need thereof comprising administering to the mammal a therapeutically effective amount of a compound of Claim 1 in combination with the PPAR $\alpha/\gamma$  dual agonist KRP-297.